Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Accelerated partial breast irradiation: executive summary for the update of an ASTRO evidence-based consensus statement.

Bibliographic Source(s)

Correa C, Harris EE, Leonardi MC, Smith BD, Taghian AG, Thompson AM, White J, Harris JR. Accelerated partial breast irradiation: executive summary for the update of an ASTRO evidence-based consensus statement. Pract Radiat Oncol. 2017 Mar-Apr;7(2):73-9. [48 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Smith BD, Arthur DW, Buchholz TA, Haffty BG, Hahn CA, Hardenbergh PH, Julian TB, Marks LB, Todor DA, Vicini FA, Whelan TJ, White J, Wo JY, Harris JR. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int J Radiat Oncol Biol Phys. 2009 Jul 15;74(4):987-1001. [98 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

 = Poor  = Fair  = Good  = Very Good  = Excellent

Assessment	Standard of Trustworthiness
NO	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
UNKNOWN	Methodologist Involvement
▮▯▯▯▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▯	Search Strategy
▮▮▮▮▯	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▮	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▮▮▯▯	External Review
▮▮▮▮▮	Updating

Recommendations

Major Recommendations

The American College of Physicians (ACP) process for assigning strength of recommendation (Strong, Weak) and grading of quality of evidence (High- [HQE], Moderate- [MQE], and Low-Quality [LQE]) is defined at the end of the "Major Recommendations" field.

Key Question (KQ) 1: Which patients may be considered for accelerated partial breast irradiation (APBI) outside of a clinical trial?

Age

Recommendation Statements

Include age greater than or equal to 50 years in the "suitable" group. (MQE, recommendation rated as "Weak")
Patients who are aged 40–49 years and who meet all other elements of suitability are considered "cautionary". (LQE, recommendation rated as "Weak")
Retain patients with age less than 40 years or those who are 40–49 years without meeting other elements of suitable in the "unsuitable" group. (No evidence rating, recommendation rated as

"Weak")

Margins

Recommendation Statement

Maintain the current selection criteria for "suitable", "cautionary" and "unsuitable" patients based on margin status (No evidence rating, recommendation rated as "Weak")

Pure Ductal Carcinoma In Situ (DCIS)

Recommendation Statement

Include patients with low-risk DCIS as per the Radiation Therapy Oncology Group (RTOG) 9804 criteria (i.e., screen-detected, low to intermediate nuclear grade, less than or equal to 2.5 cm size, resected with margins negative at ≥3 mm), in the "suitable" group. (MQE, recommendation rated as "Weak")

New Key Question: Which patients may be considered for intraoperative partial breast irradiation?

Recommendation Statements

Patients interested in cancer control equivalent to that achieved with whole breast irradiation post lumpectomy for breast conservation should be counseled that in two clinical trials the risk of ipsilateral breast cancer tumor recurrence (IBTR) was higher with intraoperative radiation therapy (IORT). (HQE, recommendation rated as "Strong")
Electron beam IORT should be restricted to women with invasive cancer considered "suitable" for partial breast irradiation (see Table 3 in the supplemental material) based on the results of a multivariate analysis with median follow up of 5.8 years. (MQE, recommendation rated as "Strong")
Low-energy x-ray IORT for partial breast irradiation (PBI) should be used within the context of a prospective registry or clinical trial, per American Society for Radiation Oncology (ASTRO) Coverage with Evidence Development (CED) statement. When used, it should be restricted to women with invasive cancer considered "suitable" for partial breast irradiation (see Table 3 in the supplemental material) based on the data at the time of this review. (MQE, recommendation rated as "Weak")

Definitions

American College of Physicians (ACP) Process for Grading of Quality of Evidence

High-Quality Evidence

Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence

Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence

Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on

confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose–response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

ACP Process for Assigning Strength of Recommendation

Strong Recommendation

Evidence suggests that the benefit of the intervention outweighs the risk, or vice versa, and the panel has reached uniform consensus.

Weak Recommendation

Evidence suggests that the benefit of the intervention equals the risk, or vice versa, and the panel has reached uniform or non-uniform consensus.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Breast cancer

Guideline Category

Management

Risk Assessment

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Radiation Oncology

Radiology

Intended Users

Physicians

Guideline Objective(s)

To update the American Society for Radiology Oncology (ASTRO) accelerated partial breast irradiation

(APBI) consensus statement, with a focus on selection criteria for APBI and intraoperative radiation therapy (IORT) for partial breast irradiation (PBI) outside of a clinical trial

Target Population

Patients 18 and older with stage I/II breast cancer following breast conserving surgery

Interventions and Practices Considered

1. Assessment of risk factors for local recurrence following use of accelerated partial breast irradiation (APBI) (age, surgical margins, patients with ductal carcinoma in situ [DCIS])
2. Considerations for use of intraoperative radiation therapy (IORT)
    - Counseling patients on risk of ipsilateral breast cancer tumor recurrence (IBTR)
    - Electron beam IORT
    - Low-energy x-ray IORT for partial breast irradiation

Major Outcomes Considered

- Risk of ipsilateral breast tumor recurrence (IBTR)
- 5-year local recurrence
- Disease-free survival
- Overall survival
- Treatment-related toxicity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Review

A systematic literature review in PubMed formed the basis of the guideline using the same terms as the original Consensus Statement (see the "Availability of Companion Documents" field). The searches identified English-language studies between May 2008 and March 2014 that evaluated patients 18 and older with stage I/II breast cancer who received accelerated radiotherapy following breast conserving surgery. Due to the complexity of the topic and the length of time to the completion of the paper, the literature search was extended to March 2016. A total of 419 articles that included the following key words were identified: Breast neoplasms/radiotherapy, accelerated, balloon, brachytherapy, catheter, implant, implantation, interstitial, intraoperative, limited, partial, Savi, Contura, TARGIT, Intrabeam, Xoft, Clearbeam, IOERT, IORT, and Mobitron. The electronic searches were supplemented by hand searches and articles suggested by the chair. The search ultimately yielded 19 randomized trials, 24 prospective studies, and 1 meta-analysis, all of which were abstracted into literature tables and made available to the task force during discussions. Retrospective studies were also discussed and cited when they provided novel information relevant to the subject matter.

Number of Source Documents

The search yielded 19 randomized trials, 24 prospective studies, and 1 meta-analysis.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American College of Physicians (ACP) Process for Grading of Quality of Evidence

High-Quality Evidence

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Moderate-Quality Evidence

Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence

Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose–response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

For each guideline statement, the strength of the supporting evidence was rated using the American College of Physicians (ACP) Process for Assigning Strength of Recommendation and Grading of Quality of Evidence. The evidence supporting respective guideline statements was rated high-quality evidence (HQE), moderate-quality evidence (MQE), or low-quality evidence (LQE) (see the "Rating Scheme for the Strength of the Evidence" field). The chair initially assigned the ratings, which the task force later approved.

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Process

In April 2014, a work group was formed to review the available evidence and recommend whether the accelerated partial breast irradiation (APBI) Consensus Statement should be updated. The work group included three coauthors of the original Consensus Statement, a breast cancer expert not involved in the initial Consensus Statement, and three members of the American Society for Radiation Oncology (ASTRO) guidelines subcommittee. After a review of the literature, the work group recommended a partial update of the Consensus Statement including: (1) revising the inclusion criteria of the "suitable" and "cautionary" patient groups, with regard to age, margins, and pure ductal carcinoma in situ (DCIS); and (2) creating a new key question regarding the use intraoperative radiation therapy (IORT) for partial breast irradiation (PBI) in early-stage breast cancer outside of a clinical trial. Other aspects of the prior guideline were felt to still be current and thus not in need of updating. The work group also proposed adding two IORT experts: a surgeon and a radiation oncologist. In January 2015, the ASTRO Board of Directors approved the proposal to partially update the Consensus Statement.

Through a series of communications by conference calls and emails between March 2015 and May 2016, the task force, with ASTRO staff support, completed the systematic review, created literature tables, and formulated the recommendation statements and narratives.

Grading of Evidence and Recommendations and Consensus Methodology

The task force consensus on the statements was evaluated through a modified Delphi approach. The task force members independently rated their agreement with each recommendation on a five-point Likert scale, from strongly disagree to strongly agree using an electronic survey. A pre-specified threshold of greater than or equal to 75% "agree" or "strongly agree" responses indicated consensus was achieved. A total of four survey rounds, with revision as needed after each survey, were conducted to ascertain consensus on all the recommendation statements.

For each statement, the strength of the recommendation was rated using the American College of Physicians (ACP) process for Assigning Strength of Recommendation and Grading of Quality of Evidence (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). In determining recommendation strength, balance of risks and benefits was assessed. The chair initially assigned the ratings, which the task force later approved. A strong recommendation was defined as the benefit of the intervention outweighs the risk, or vice versa, with uniform consensus. A weak recommendation was defined as the benefit of the intervention equals the risk, or vice versa, with uniform or non-uniform consensus.

Rating Scheme for the Strength of the Recommendations

American College of Physicians (ACP) Process for Assigning Strength of Recommendation

Strong Recommendation

Evidence suggests that the benefit of the intervention outweighs the risk, or vice versa, and the panel has reached uniform consensus.

Weak Recommendation

Evidence suggests that the benefit of the intervention equals the risk, or vice versa, and the panel has reached uniform or non-uniform consensus.

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The initial draft was reviewed by four expert reviewers and the American Society for Radiation Oncology (ASTRO) legal counsel. A revised draft was placed on the ASTRO Web site in February 2016 for public comment. Following integration of the feedback, the document was submitted for approval to the ASTRO Board of Directors July 2016. The ASTRO guidelines subcommittee will reevaluate this update when necessary.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- It is hoped that this update will provide ongoing direction for radiation oncologists and other specialists participating in the care of breast cancer patients.
- When compared with whole breast irradiation (WBI), all accelerated partial breast irradiation (APBI) and intraoperative radiation therapy (IORT) for partial breast irradiation (PBI) strategies offer several benefits, including reduced treatment time and sparing of uninvolved tissue.

Potential Harms

- Adverse effects are different after intraoperative radiation therapy (IORT) compared with whole breast irradiation (WBI). In the available trials, fat necrosis was increased with IORT, while skin side effects were lower. Mild breast fibrosis occurred with electron beam radiation on ELIOT, with no significant difference compared to WBI in the ELIOT trial. IORT techniques may allow improved critical organ sparing compared to WBI. Lung fibrosis in the ELIOT trial and deaths from cardiovascular causes in the TARGIT trial were lower in the IORT groups.
- In some studies, breast fibrosis was problematic for the combination of low-energy x-rays followed by WBI. For example, the use of low-energy x-ray IORT followed by WBI, compared to WBI alone, was associated with double the risk of breast fibrosis (to 37.5%), increased patient-reported pain, and decreased patient-reported quality of life. In contrast, other studies have reported outcomes with IORT followed by WBI that appear acceptable and comparable to either WBI alone or WBI with

a conventional external beam boost. As such, the task force felt that the combination of IORT and WBI should be used only with caution and limited to women with higher risk features on final pathology.
- Several key studies have provided important new data on the complication profile of accelerated partial breast irradiation (APBI) delivered with external beam radiation therapy (3-dimensional conformal radiation therapy [3D-CRT]) or intensity modulated radiation therapy (IMRT). Although the IBTR risk has not yet been reported, cosmetic outcome as assessed separately by patients, nurses, and physician panels was consistently worse at 3 and 5 years in patients randomized to 3D-CRT APBI. Single-arm studies have also reported higher rates of fair-poor cosmetic outcomes in approximately 20% of patients treated with EBRT-based APBI, while other clinical series of APBI delivered with 3D-CRT or IMRT reported acceptable cosmetic outcomes.

Qualifying Statements

Qualifying Statements

- American Society for Radiation Oncology (ASTRO) guidelines present scientific, health, and safety information and may to some extent reflect scientific or medical opinion. They are made available to ASTRO members and to the public for educational and informational purposes only. Any commercial use of any content in this guideline without the prior written consent of ASTRO is strictly prohibited.
- Adherence to this guideline will not ensure successful treatment in every situation. Furthermore, this guideline should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all circumstances presented by the individual patient. ASTRO assumes no liability for the information, conclusions, and findings contained in its guidelines. In addition, this guideline cannot be assumed to apply to the use of these interventions performed in the context of clinical trials, given that clinical studies are designed to evaluate or validate innovative approaches in a disease for which improved staging and treatment are needed or are being explored.
- This guideline was prepared on the basis of information available at the time the task force was conducting its research and discussions on this topic. There may be new developments that are not reflected in this guideline update, and that may, over time, be a basis for ASTRO to consider revisiting and updating the guideline.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Correa C, Harris EE, Leonardi MC, Smith BD, Taghian AG, Thompson AM, White J, Harris JR. Accelerated partial breast irradiation: executive summary for the update of an ASTRO evidence-based consensus statement. Pract Radiat Oncol. 2017 Mar-Apr;7(2):73-9. [48 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Mar-Apr

Guideline Developer(s)

American Society for Radiation Oncology - Professional Association

Source(s) of Funding

American Society for Radiation Oncology

Guideline Committee

Accelerated Partial Breast Irradiation Update Task Force

Composition of Group That Authored the Guideline

Task Force Members: Candace Correa, MD, Department of Radiation Oncology, Faxton St. Luke's Healthcare, Utica, NY; Eleanor E. Harris, MD, Department of Radiation Oncology, East Carolina University, Greenville, NC; Maria Cristina Leonardi, MD, Department of Radiation Oncology, European Institute of Oncology, Milan, Italy; Benjamin D. Smith, MD, Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; Alphonse G. Taghian, MD, PhD, Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA; Alastair M. Thompson, MD, Department of Breast Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; Julia White, MD, Department of Radiation Oncology, Ohio State University Cancer Center, Columbus, OH; Jay R. Harris, MD, Department of Radiation Oncology, Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA

Financial Disclosures/Conflicts of Interest

Before initiation of this update, all members of the Update Task Group were required to complete disclosure statements. These statements are maintained at American Society for Radiation Oncology (ASTRO) Headquarters in Arlington, VA, and pertinent disclosures are published with this report. The ASTRO Conflict of Interest Disclosure Statement seeks to provide a broad disclosure of outside interests. Where a potential conflict is detected, the disclosure and any remedial measures to address potential conflicts are taken and noted in the consensus statement.

Benjamin D. Smith, MD receives research funding from Varian Medical Systems. Maria Cristina Leonardi, MD holds position of the National Coordinator of IORT Working Group on behalf of the Italian Society of Radiation Oncology and is the co-investigator in an ongoing boost IORT. She is also the author of three and co-author of twelve papers on IORT. Alastair M. Thompson, MD is a site principal investigator for the TARGIT- A trial and co-author for the resulting publication. Eleanor E. Harris, MD is the writing committee member for the TARGIT-A trial and a co-author for the resulting publication. She is also a principal investigator for the NRG institutional and committee member for the NRG Breast Cancer Working Group. Julia White, MD receives research funding from Susan G. Komen foundation and IntraOp Medical and paid travel expenses and research funding from Qfix. She is also a member of the National Cancer Institute (NCI) Breast Cancer Steering Group and a member-liaison of the NCI Breast Cancer Local Disease Task Force. Candace Correa, MD is a steering committee member of the Early Breast Cancer Trialists Collaborative Group (EBCTCG). None of the relationships disclosed were viewed as having any substantive impact upon the consensus statement.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Smith BD, Arthur DW, Buchholz TA, Haffty BG, Hahn CA, Hardenbergh PH, Julian TB, Marks LB, Todor DA, Vicini FA, Whelan TJ, White J, Wo JY, Harris JR. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int J Radiat Oncol Biol Phys. 2009 Jul 15;74(4):987-1001. [98 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Practical Radiation Oncology Web site .

Availability of Companion Documents

The following are available:

Correa C, Harris EE, Leonardi MC, Smith BD, Taghian AG, Thompson AM, White J, Harris JR. Accelerated partial breast irradiation: update of an ASTRO evidence-based consensus statement. Supplementary material. Pract Radiat Oncol. 2017 Mar-Apr. 26 p. Available from the Practical Radiation Oncology Web site .

Smith BD, Arthur DW, Buchholz TA, et al. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int J Radiat Oncol Biol Phys. 2009;74(4):987-1001. Available from the International Journal of Radiation Oncology Biology Physics Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 24, 2012. The information was verified by the guideline developer on August 22, 2012. This summary was updated by ECRI Institute on May 12, 2017. The updated information was verified by the guideline developer on June 7, 2017.

This NEATS assessment was completed by ECRI Institute on June 22, 2017. The information was verified by the guideline developer on July 11, 2017.

Copyright Statement

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